RESEARCH ON HERITABLE DISORDERS OF CONNECTIVE TISSUE

NIH GUIDE, Volume 21, Number 12, March 27, 1992

PA NUMBER: PA-92-64

P.T. 34

Keywords:
Musculoskeletal System
Genetics
Disease Model
Clinical Medicine, General

National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Child Health and Human Development

PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and National Institute of Child Health and Human Development (NICHD) invite grant applications for basic and clinical research projects on heritable disorders of connective tissue.

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, non-profit and for-profit, public and private organizations, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. However, foreign institutions are not eligible for the First Independent

Research Support and Transition (FIRST) Award (R29) and the career development awards (K04, K08, K11). Applications from minority individuals and women are encouraged.

MECHANISM OF SUPPORT

Support will be offered through research projects grants (R01), FIRST awards (R29), fellowship training (F32, F33, T32), and career development awards (K04, K08, K11).

RESEARCH OBJECTIVES

Over 200 distinct disorders are recognized as being caused by mutations in genes that encode matrix proteins or in genes that ultimately affect the structure of the extracellular matrix. Collectively, these disorders are termed heritable disorders of connective tissue. There is a wide range of anatomic sites and clinical manifestations that can result from these conditions. In total, it is estimated that heritable disorders of connective tissue account for major and, in some cases, life-threatening illnesses in approximately half a million people in the United States.

Some mutations in genes may give rise to severe abnormalities, while others may produce milder symptoms. There is also recent scientific evidence that mild phenotypes may appear in more common disorders, such as osteoarthritis and osteoporosis.

On April 9-11, 1990, the NIAMS, the NICHD, and the Coalition for Heritable Disorders of Connective Tissue sponsored a Workshop on Heritable Disorders of Connective Tissue at the National Institutes of Health. The focus of the Workshop was to review the current status of research in this field and to identify important directions for future research. Major advances have been achieved in identifying molecular components of the extracellular matrix, in isolating and characterizing the genes that encode these proteins, in defining biosynthetic pathways and interactions between proteins, and in characterizing specific mutations in some disease categories.

The Workshop participants described the need for continued integration of insights gained from collaborative research perspectives, such as molecular biology, biochemistry, physical biochemistry, anatomy, and clinical genetics, the need to identify cohorts of patients and families with rare disorders, and the need to recognize structure-function relationships in interpreting genetic mutations. Some broad areas of recommended research directions include, but are not limited to:

- Identification and characterization of mutations in many disease phenotypes;

- Structure-function relationships of normal matrix molecules;

- Developmental regulation of matrix formation;

- Multi-disciplinary analysis of disease mechanisms;

o Clinical studies: natural history and clinical trials in these disorders;

o Identification and study of animal models using transgenic technologies;

o Application of genetic linkage strategies to these inherited disorders;

o Pursuit of the molecular/genetic basis of selected common diseases.

The above examples of research areas related to heritable disorders of connective tissue are not presented in a priority order and are not intended to restrict the wide range of meritorious areas in which investigators may apply. A complete report of the 1990 Workshop is available upon request from Dr. Stephen L. Gordon at the address below.

STUDY POPULATIONS

SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 in Section 2, 1-4 of the Research Plan and summarized in item 5, Human Subjects. Applicants/offerors are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders,

Blacks, Hispanics). The rationale for studies on single minority population groups must be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including, but not limited to, clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be ddressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the review will be deferred until the information is provided.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed and the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

APPLICATION PROCEDURES

Applications are to be submitted on the grant application form PHS 416- 1 (rev. 4/89) for individual fellowships, for other awards use PHS 398 (rev. 9/91) and will be accepted at the standard application deadlines indicated in the application kit.

Application kits are available at most institutional business offices and may be obtained from the Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892, telephone 301/496-7441. The title and number of the announcement must be typed in Section 2a on the face page of the PHS 398.

The completed original application and five legible copies of the PHS 398 or two copies of the PHS 416-1 must be sent or delivered to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

REVIEW PROCEDURES

Applications will be assigned on the basis of established Public Health Service referral guidelines. Applications will be reviewed for scientific and technical merit by initial review groups of the Division of Research Grants, NIH, or by the review group of the relevant Institute, Center, or Division (ICD), in accordance with the standard NIH peer review procedures. Following scientific-technical review, the applications will receive a second-level review by the appropriate national advisory council.

AWARD CRITERIA

Applications will compete for available funds with all other approved applications assigned to that ICD. The following criteria will be considered in making funding decisions:

o Quality of the proposed project as determined by peer review;

o Availability of funds;

o Program balance among research areas of the announcement.

INQUIRIES

Written and telephone inquiries are encouraged. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries for the NIAMS regarding programmatic issues to:

Stephen L. Gordon, Ph.D.
Chief, Musculoskeletal Diseases Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 407
Bethesda, MD 20892
Telephone: (301) 496-7495

Direct inquiries for the NICHD regarding programmatic issues to:

Delbert Dayton, M.D.
Chief, Genetics & Teratology Branch
National Institute of Child Health and Human Development
Executive Plaza North, Room 643
Rockville, MD 20892
Telephone: (301) 496-5541

Direct inquiries for the NIAMS regarding fiscal matters to:

Ms. G. Carol Clearfield
National Institute of Arthritis and Musculoskeletal and Skin Diseases
5333 Westbard Avenue, Room 726B
Bethesda, MD 20892
Telephone: (301) 496-6529

Direct inquiries for the NICHD regarding fiscal matters to:

Douglas Shawver
National Institute of Child Health and Human Development
Executive Plaza North, Room 505
Rockville, MD 20892
Telephone: (301) 496-1303

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846, Arthritis, Musculoskeletal and Skin Disease Research, 93.862, Genetics Research, 93.865, Research for Mothers and Children. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78- 410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

Return to 1992 Index

Return to NIH Guide Main Index